

Amendments to the Specification:

On page 8, line 4, please insert the following:

[0024] It has been hypothesised that Activation-Induced Cytidine Deaminase activity would be restricted to the physiological target (the immunoglobulin loci) because rampant DNA deaminase activity would be harmful to the cell. There is some suggestion that the deaminase activity of Activation-Induced Cytidine Deaminase is sequence specific (30), and it is hypothesised that Activation-Induced Cytidine Deaminase would show greatest activity on the somatic hypermutation hot-spot sequence RGYW; SEQ ID NO: 14 (a sequence commonly mutated in the variable region of the immunoglobulin gene). Bransteitter et al. (27) showed that in vitro Activation-Induced Cytidine Deaminase had approximately three-fold higher activity on two hot-spot sequences compared with non-hot-spot sequences. Conversely, Dickerson et al. (26) found that the deaminase activity of Activation-Induced Cytidine Deaminase was sequence specific, but that cold-spot sequences (sequences of the variable region of the immunoglobulin gene that have never been found to be mutated in vivo) were deaminated equally well as hot-spot sequences, and that some hot-spot sequences were deaminated at only background levels.

On page 26, line 20, please insert the following:

[0107] An unmethylated 80 bp oligonucleotide (Ecad80) which has the same nucleotide sequence as nucleotide bases #920 to #999 of the E-cadherin promoter

region (GenBank Accession #L34545), was diluted to 4 .mu.M in 50 mM NaCl.

The sequence of Ecad80 is as follows: 5' cgc tgc tga ttg gct gtg gcc ggc agg tga acc
ctc agc caa tca gcg gta Cgg ggg gcg gtg ctc cgg ggc tca cct gg 3'; SEQ ID NO: 1.

Nucleotide base #52 in this sequence (upper case C) was screened with the
primer 3ECAD11b in the cycle sequencing primer extension assay described
below in D, and corresponds to base #972 of E-cadherin promoter region
(GenBank Accession # L34545).

On Page 26, line 24, please insert the following:

[0108] Complementary oligonucleotides AA1 (tgt ttt ggg tgt gta tgg ttt ggg tgt);
SEQ ID NO: 2 and AA2 (aca ccc aaa cca tac aca ccc aaa aca); SEQ ID NO: 3 were
diluted to 30 .mu.M each in 20 mM NaCl and the mixture was heated to
95.degree. C. for 5 min, and cooled slowly to room temperature to allow
annealing of the complementary strands. The resulting double stranded "TRAP
DNA" template was used as a decoy for exonuclease activity in the following 20
.mu.L AID reaction mixture.

On page 27, line 19, please insert the following:

[0111] In these reactions, 4 .mu.L of AID modified substrate was amplified using
a cycle sequencing protocol. Specifically, cycle sequencing reactions contained
1.times. Thermosequenase buffer (USB), 3 Units of Thermosequenase (USB), 67
nM .sup.32P-end labelled primer 3ECAD11b (5' agc ccc gga gca ccg ccc 3')[[7]];

SEQ ID NO: 15, 80 .mu.M each of ddATP, dGTP, dCTP and dTTP, and 20 mL mineral oil. The primer 3ECAD11b screens base #972 in the E-cadherin promoter region (GenBank Accession # L34545) of genomic DNA or base #52 in Ecad80. Reactions were thermocycled for 7 cycles of (95.degree. C. for 30 s, 55.degree. C. for 45 s, 72.degree. C. for 5 min). Reactions were stopped with 10 .mu.L stop solution containing 95% form amide, 10 mM EDTA, 0.1% xylene cyanol and 0.1% bromophenol blue, denatured at 95.degree. C. for at least 2 minutes and placed immediately on ice. Products were separated on a 20% polyacrylamide gel which was run for 3 hours at 60 W prior to being dried. Quantitation of the band intensities provides an estimate of the percentage of target template that has been deaminated at position #972.

On page 29, lines 5 and 6, please insert the following:

[0114] DNA oligonucleotides were chemically synthesized with the following sequence: cgc tgc tga ttg gct gtg gcX.sub.1 ggc agg tga acc ctc agc caa tca gX.sub.2g gta X.sub.3gg ggg gcg gtg ctc cgg ggc tca cct gg, where X was either unmodified (Ecad80--all cytosine); SEQ ID NO: 1 or 5'-methylcytosine (5'-MeC) modified (Ecad80M3--containing three 5-MeC bases at X.sub.1, X.sub.2 and X.sub.3); SEQ ID NO: 4. Ecad80 or Ecad80M3 were diluted to 4 uM (in the presence of 50 mM NaCl).

On page 29, lines 9 and 10, please insert the following:

[0115] Complementary oligonucleotides T1 (att ata ttt aaa tat ata aaa tat ata tta ata aat); SEQ ID NO: 5 and T2 (att tat taa tat ata ttt tat ata ttt aaa tat aat); SEQ ID NO: 6, were diluted to 30 .mu.M each in the presence of 20 mM NaCl. These oligonucleotides were annealed to function as TRAP DNA as described in Example 3.

On page 31, line 14, please insert the following:

[0123] Ecad80 was diluted to 4 .mu.M in 50 mM NaCl with three-fold excess of ASEcad80 which is the antisense sequence of Ecad80 (ASEcad80 sequence: 5' cc agg tga gcc ccg gag cac cgc ccc ccg tac cgc tga ttg gct gag ggt tca cct gcc ggc cac agc caa tca gca gcg 3'); SEQ ID NO: 7. Mixtures were heated to 95.degree. C. for 5 minutes and cooled slowly to room temperature to allow annealing of complementary strands.

On page 31, lines 22 and 24, please insert the following:

LP10 - 5' CGA CCG CCC CGA TTG GCT GAG G 3' (with 3' phosphate); SEQ ID NO: 8

LP26 - 5' GCC CCG GAG CGA GGG TTC ACC TG 3' (with 3' phosphate); SEQ ID NO: 9 and

On page 32, line 1, please insert the following:

LP26 + 1 - 5' GCC CCG GAG CGG AGG GTT CAC CTG 3' (with 3' phosphate);

SEQ ID NO: 10.

On page 33, line 9, please insert the following:

[0130] Ecad80 (5' cgc tgc tga ttg gct gtg gcc ggc agg tga acc ctc agc caa tca gcg gta
Cgg ggg gcg gtg ctc cgg ggc tca cct gg 3'); SEQ ID NO: 1 was diluted to 4 .mu.M in
50 mM NaCl.